

## Evolving Technology

# Percutaneous aortic valve replacement: An experimental study. I. Studies on implantation

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Dr. Lutter is supported by the Clinical Cardiovascular Research Center II and III at the Medical Center (grant B3 and 11-00-III), Albert-Ludwigs-University of Freiburg, Germany.

Read at the Eighty-first Annual Meeting of The American Association for Thoracic Surgery, San Diego, Calif, May 6-9, 2001.

Received for publication May 15, 2001; revisions requested Sept 14, 2001; revisions received Oct 1, 2001; accepted for publication Oct 8, 2001.

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J Thorac Cardiovasc Surg 2002;123:768-76

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0022-5223/2002 \$35.00+0 12/6/121157

doi:10.1067/mtc.2002.121157

**Objective:** The purpose of this preliminary study was to devise a new surgical procedure for minimally invasive aortic valve implantation with a transluminal technique.

**Methods:** The new collapsible heart valve was prepared by mounting a porcine aortic valve, taken from a freshly slaughtered pig, into a self-expandable nitinol stent by means of a suture technique. The outer diameter of the valved stent ranged from 15 to 23 mm, and the length ranged from 21 to 28 mm. Before implantation in vivo, these valved stents were tested in an in vitro circulatory system. Only in vitro-tested valved stents with a pressure gradient of less than 7 mm Hg and regurgitation of I° or less were used for transluminal aortic valve implantation in vivo. Six of these valved stents were implanted in the descending aorta and 8 in the ascending aorta of anesthetized pigs. The catheter delivery system (22F) was extraperitoneally inserted through the left iliac artery or the infrarenal aorta. Measurements for transvalvular gradient, valvular opening and closure, blood-flow characteristics, regurgitation, and macroscopic analysis were performed at baseline and after the observation period ( $164 \pm 48$  minutes).

**Results:** This preliminary study contained 14 animals. One animal died of ventricular fibrillation. Technical failure occurred in 2 pigs as a result of stent twisting. At the end of the observation period, the 11 successfully implanted valved stents demonstrated low transvalvular gradients (mean end-systolic  $\Delta p_{\max}$  of  $5.4 \pm 3.3$  mm Hg for the descending aorta group,  $5.4 \pm 1.2$  mm Hg for the supracoronary group, and  $5.4 \pm 1.1$  mm Hg for the subcoronary group), which did not differ from their in vitro gradients. Two-dimensional echocardiography demonstrated complete valvular closure and opening in 5 of 5 cases. Angiography indicated only a physiologic jet of regurgitation (0°) in 8 animals and mild (I°) regurgitation in 3 animals. Color Doppler ultrasonography indicated no regurgitation in 5 of 5 cases and minor paravalvular leakage in 1 case.

**Conclusion:** Aortic valved stents can be successfully implanted without thoracotomy by using a transluminal catheter technique. Long-term function of the valves remains to be established.

**A**ortic valve replacement generally has been accomplished by using a cardiac surgical procedure, whereas endovascular procedures for valve replacement may provide an alternative to cardiac surgery. Percutaneous transluminal procedures have substantial benefits from the standpoints of health and safety, as well as from the standpoint of cost. Such endovascular procedures require minimal

invasion of the human body, and there is considerable reduction and, in some instances, even elimination of general anesthesia and intensive care unit stay.

A number of minimally invasive techniques for replacing heart valves have been experimentally developed over the last 10 years. Such techniques have been reported by Andersen and coworkers,<sup>1</sup> who indicated in 1992 that artificial aortic valves can be implanted in closed-chest animals by means of a transluminal catheter technique; by Pavcnik and colleagues,<sup>2</sup> who demonstrated in 1992 that a percutaneous transcatheter placement of an artificial caged-ball valve in animals is feasible; by Maozami and coworkers,<sup>3</sup> who showed in 1996 that a hemodynamically acceptable prosthetic aortic valve for transluminal placement is feasible, whereas an open chest model for implantation was used; and by Bonhoeffer and coworkers<sup>4</sup> in 2000, who successfully performed a percutaneous pulmonary valve implantation in 5 sheep. Although the instruments, devices, and techniques reported are clearly experimental, it appears that each of them still has one or more problems.

It would be especially advantageous if a defective heart valve could be removed by means of an endovascular procedure (ie, through the femoral artery). The procedure is then carried out percutaneously and transluminally by using the vascular system to convey appropriate devices to the aortic anulus to carry out the percutaneous aortic valve ablation procedure.

We set out to develop a technique for placement of a biologic valve in the aortic position through a transluminal approach.<sup>5</sup> This report presents our initial experience with transluminal aortic valve implantation in the circulatory system of anesthetized pigs after this experimental set up had been developed in more than 30 pilot studies.

## Materials and Methods

### Experimental Preparation

**Production of valved stents.** Eleven of the 14 animals received homologous valves. These aortic valves were harvested from fresh porcine cadavers. Seventy percent ethanol solution was used for transport. The aortic wall of the harvested valve section was trimmed to remove extraneous material and to reduce the size (by D.K.). However, sufficient material had to remain to allow permanent valve configuration and safe attachment of the aortic valve to the stent.

Pericardial valves were used in the other 3 animals. Pericardium of the same animals was selected for the creation of valves. Pericardium was cleaned, prepared, preserved with glutaraldehyde (0.6%), and finally constructed with an ultra-thin polytetrafluoroethylene layer to the exterior for stabilization (by D.K.).

The above-described valves were sutured to the interior of a stent with 7-0 polypropylene sutures. This radially self-expanding vascular memory stent (21–28 mm in length and 15–23 mm in diameter) includes several cylindrical fine-wire sections that are interconnected into a single tubular structure. The size of the valved stent correlated with the width of the aorta (as determined

with intra-arterial digital subtraction angiography [IA-DSA]) and body weight. The wires are made of a soft and highly malleable alloy consisting of nitinol (Nitinol Devices & Components Inc, Fremont, Calif). The tubular portion of the trimmed ascending aorta of the stentless aortic valve spanned the partial axial length of the nitinol stent (Figure 1). For the anchoring fixation, barbs are attached to the outside of the stent.

The valved stent was finally cross-linked with a buffered saline solution containing 0.6% glutaraldehyde for 24 hours at 4°C. After fixation, it was transferred to a 70% ethanol solution for storage. Before implantation, the valve stent was immersed multiple times for 15 minutes and carefully rinsed in physiologic saline solution to remove the ethanol.

**Catheter delivery system.** The valved stent is inserted by means of a self-constructed, flexible, catheter-based (external diameter, 22F) delivery technique (overall length, 90 cm) through the iliac artery or the infrarenal aorta (Figure 2).

### In Vitro Studies

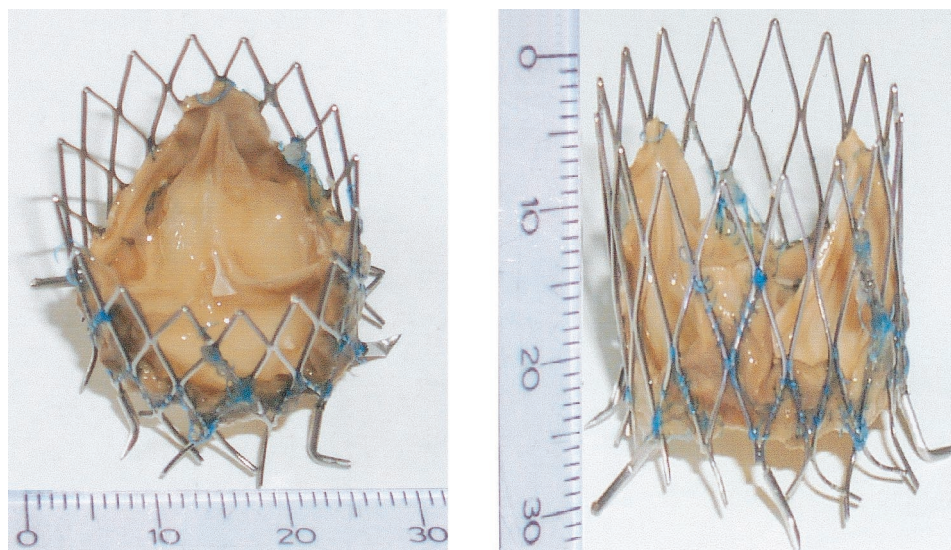
An in vitro circulatory system (hydrodynamic pulsatile-flow testing referring to the ISO norm 5840:1996-11-01) was used for the evaluation of the valved stents. This system (Figure 3) uses a pump (Stöckert-HLM, 10-40-00; Stöckert Instruments Inc, Munich, Germany) with an external flow controller (PFC-1) to generate pulsatile flow (maximum, 6.0 L/min). Each stroke ejects 63 to 75 mL of saline solution into the circuit. The system possesses an open reservoir and a compliance chamber to simulate the venous and arterial systems, respectively. In addition, peripheral vascular resistance was adjusted by using a blood-flow regulator to the circuit to partially impede forward flow. The valve was placed into a soft silicone tube with the same diameter as the aorta of the pigs used for the in vivo experiments (15–23 mm). An ultrasonic probe (Toshiba SSH 140A, 5-MHz transesophageal probe; Toshiba GmbH, Neuss, Germany) was placed on the outflow tubing to assess valve function. All data were digitized and recorded with the IBM-Lab system (IBM Inc, New York, NY).

The unitary tubular structure (Figure 1) was reduced in profile (foldable biologic valve inside a self-expanding memory stent) and placed on a catheter delivery system. During artificial circulation, the self-prepared valved stents were transluminally implanted through a 24F port into the valve chamber (Figure 3). The positioning of the valved stents into the valve chamber was enabled by means of direct view through a transparent silicone tube. The observation period in vitro lasted for 4 hours.

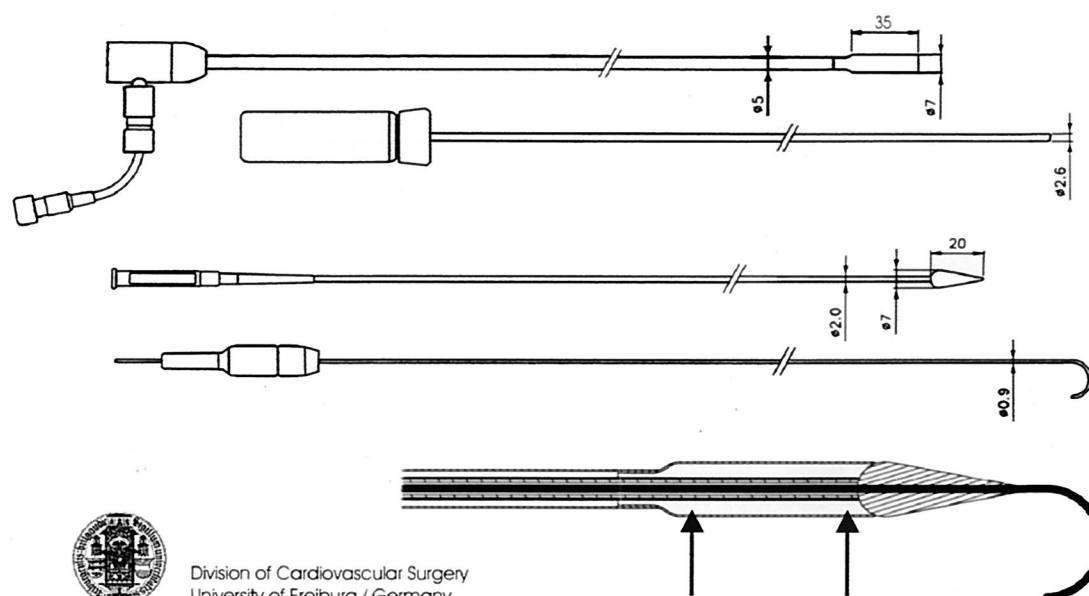
### In Vivo Studies

Animals received humane care, as approved by the Center for Experimental Animal Research at Freiburg University and in compliance with the “Guide for the Care and Use of Laboratory Animals” prepared by the Institute of Laboratory Animal Resources, National Research Council, and published by the National Academy Press, revised 1996.

Pigs of the “German Landrace” weighing 64 to 76 kg were premedicated and anesthetized, as reported elsewhere.<sup>6</sup> Only in vitro–tested valved stents with a pressure gradient of less than 7 mm Hg and a regurgitation of I° or less were used for transluminal aortic valve implantation in vivo. First, a paracolic incision and an extraperitoneal approach toward the infrarenal aorta, aortic bifur-



**Figure 1.** View of the homologous valved segment in a vascular memory stent. Note: The anchoring barbs at the outside of the valved stent ascertain the desired position after embedding.

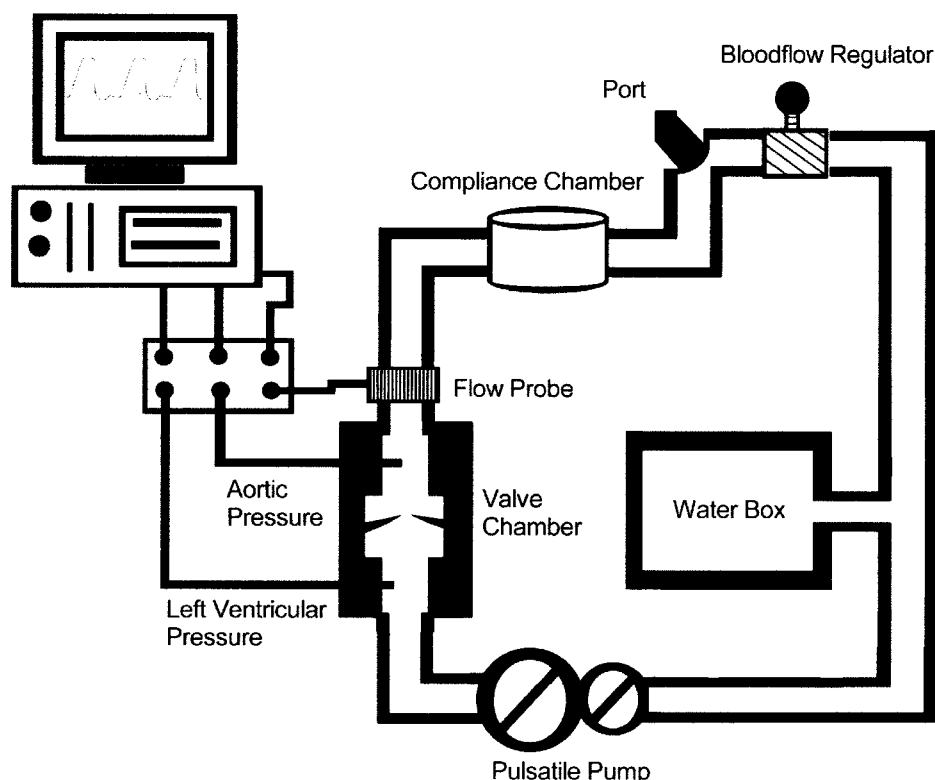


**Figure 2.** Catheter delivery system with guidewire, pusher, and external sheath. Note: The valved stent (21-28 mm in length) was hand crimped onto the proximal portion (35 mm in length) of a catheter delivery system (into the proximal capsule between the arrows).

cation, or the left iliac artery was prepared. This extraperitoneal access was chosen because femoral arteries of pigs weighing 65 to 75 kg are only 2.5 to 4.0 mm in diameter.

Second, through the iliac communis artery ( $n = 3$ ), the infrarenal aorta ( $n = 10$ ), or the iliac external artery ( $n = 1$ ), a guidewire was retrogradely positioned into the proximal descending aorta or the left ventricle under continuous fluoroscopy. The valved stent (21-28 mm in length, Figure 1) was then hand crimped onto the proximal portion (35 mm in length) of a catheter delivery

system (Figure 2). The diameter of the memory stent was dependent on body weight, and the diameter of the ascending or descending aorta was measured by using IA-DSA. The appropriate size of the valved stent was chosen from different available stent diameters, ranging from 15 to 23 mm. Because of the expandable character of the valved stent, minimal oversizing (1-2 mm) did not affect optimal valve function. The assembly was front loaded in a 22F long sheath to enable a precise positioning (Figure 2). In case of deployment into the ascending aorta, the ostia of the coronary



**Figure 3. Diagram of the hydrodynamic pulsatile-flow testing used for the in vitro testing of valved stents. The system enables the adjustment of compliance and resistance.**

arteries were identified by means of angiography for correct placement of the valved stents. The valved stent was placed at a secure distance of several millimeters from the coronary ostia into the ascending aorta (supra-annular placement) and from the native aortic valve into the left ventricular outflow tract (subannular placement).

Third, after loading onto the previously positioned guidewire, the whole system was advanced and inserted into the iliac artery or infrarenal aorta through a 24F port. The position of the valved stent was easily tracked fluoroscopically (highly radiopaque stent material) and supported by means of transesophageal echocardiography (SSH-140A, Toshiba GmbH). The valved stent was slowly released (memory stent) by pulling the securing sheath back and deployed in the ascending (subcoronary or supracoronary position) or proximal descending (distal to the subclavian artery) aorta. The duration of deployment was  $1.7 \pm 1.2$  minutes. Through the self-expanded valved stent, the catheter delivery system was subsequently pulled back and removed, leaving the valve assembly in the desired position. After deployment of the valved stent, the observation period of all experimental groups lasted  $164 \pm 48$  minutes (range, 90-240 minutes). Data were obtained for all parameters at baseline and at the end of the observation period.

### Experimental Groups

Over a 2-year period, the in vitro and in vivo experimental model gradually evolved. After the first successful implantations of a valved stent in the pilot studies ( $n = 30$ , for details see "Discus-

sion" section), the present preliminary study was started. The 14 animals fulfilled the following inclusion criteria: First, these valved stents demonstrated adequate performance in the in vitro experiments, and second, before implantation of these valved stents, their catheter delivery system has been successfully tested.

In the descending aorta group the in vitro-controlled homologous valved stents (21-28 mm in length,  $n = 6$ ) were implanted into the proximal descending aorta (distal to the subclavian artery).

In the supracoronary group valved stents ( $n = 6$ , 28 mm of length) were implanted into the proximal ascending aorta (distal to the coronary ostia) of the anesthetized pigs.

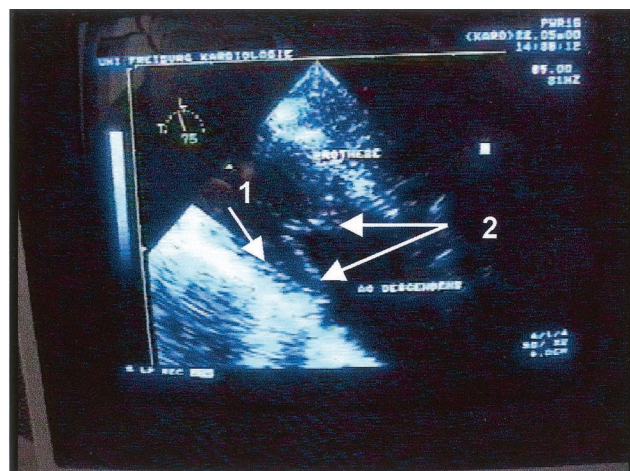
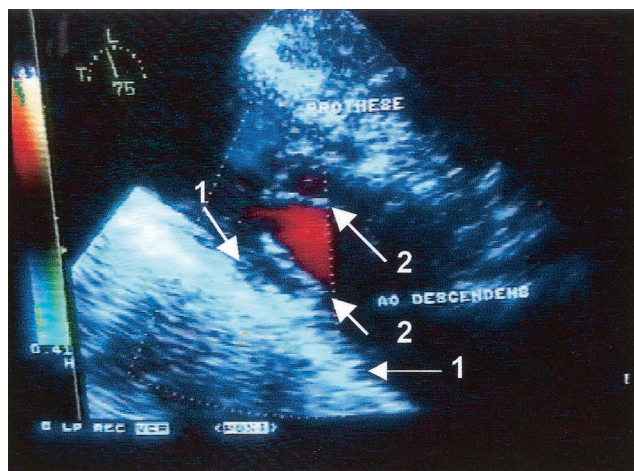
In the subcoronary group 2 pigs received valved stents into the left ventricular outflow tract (shortly beyond the native valve), with a shorter stent of 21 mm in length.

### Measurements

**Assessment of transvalvular gradient.** In vitro, pressure transducers that were placed on the ventricular and the aortic side of the valved stent were used to analyze the transvalvular gradient shortly after implantation and after 4 hours (by D.K.). In vivo, blood pressure was measured online with two 5F Millar micromanometers placed in the proximal and distal area of the deployed valved stent.

**Evaluation of valvular opening and closure.** Two-dimensional ultrasonography in vitro (by D.K.) and 2-dimensional transesophageal echocardiography in vivo (by M.H.) were used to semiquantitatively grade the valvular opening and closure process





**Figure 4.** In vivo evaluation of a homologous valved stent in the descending aorta under transesophageal echocardiography control. Note: There is good visualization of the laminar transvalvular blood flow (left) and the fully closed leaflets of the new valve (right). 1, Nitinol stent; 2, valve cusp.

(0, total valvular opening and closure; I, partial opening or incomplete closure of one or more leaflets; II, lack of movement of one leaflet; and III, lack of movement of 2 or more leaflets; Figure 4).

**Blood-flow characteristics.** Color Doppler ultrasonography was used to examine, in vitro (by D.K.) and in vivo (by M.H.), the blood-flow supralvalvular, intravalvular, and subvalvular characteristics of the valved stent.

**Regurgitation and paravalvular leakage.** Color Doppler ultrasonography in vitro (by D.K.) and in vivo (by M.H.) and additional angiography in vivo were used to assess any valve insufficiency (0, no; I, mild; II, moderate; III, severe; and IV, fulminant regurgitation) and paravalvular leakage (0, none; I, mild; II, moderate; III, severe; and IV, fulminant leakage).

**Mortality and complications.** All complications (mechanical and others) and deaths were identified.

**Duration of deployment.** The time from pushing the valved stent out of the cranial catheter capsule (Figure 2) and the total deployment into the left ventricular outflow tract or aortic lumen was recorded.

**Macroscopic analysis.** First, the desired positioning of the valved stent in situ was controlled (0, optimal positioning; I, <5 mm; II, >5 mm; III, >10 mm from the desired position). Second, the anchoring of the valved stents was determined in situ (0, sufficient anchoring; I, minimal shift; II, moderate shift; and III, twisting of the valved stent). Third, all grafts were explanted. Fourth, the valved stent was rinsed with distilled water to remove the blood and was macroscopically inspected. Gross leaflet structure and integrity were analyzed, referring to the grading of morphologic damage (0, no; I, mild; II, moderate; and III, severe morphologic damage) and thrombus formation (0, none; I, small; II, moderate; and III, fulminant thrombus formation).

### Statistical Analysis

Paired and unpaired *t* tests with the Bonferroni correction were used as appropriate. Values are reported as means  $\pm$  SD. Data were used from all animals who survived the entire observation

period ( $n = 11$ ). Only data of valved stents that demonstrated sufficient anchoring ( $0^\circ$ - $I^\circ$ ) were analyzed.

## Results

### In Vitro Studies

**Assessment of transvalvular gradient.** After 4 hours in the hydrodynamic pulsatile-flow testing, the homologous valved stents demonstrated a pressure gradient of less than 7 mm Hg (mean end-systolic transvalvular gradient  $\Delta p_{\max}$ ,  $4.5 \pm 1.7$  mm Hg) and pericardial valved stents (mean end-systolic  $\Delta p_{\max}$ ,  $5.9 \pm 1.4$  mm Hg) were revealed. In addition, different pressure values compared with baseline were not observed.

**Evaluation of valvular opening and closure.** Semi-quantitative assessment of the valvular opening and closure process demonstrated total valvular opening and closure in all cases.

**Blood-flow characteristics.** Color Doppler ultrasonography demonstrated systolic laminary blood flow in all cases (supralvalvular, intravalvular, and subvalvular).

**Regurgitation and paravalvular leakage.** Minimal regurgitation was observed in 3 cases ( $0^\circ$ - $I^\circ$ ), whereas in 11 cases valve insufficiency was excluded ( $0^\circ$ ). Paravalvular leakage occurred in 3 of the cases because of a short distance between the valved stent and silicone tube caused by the barbs.

### In Vivo Studies

**Mortality and complications.** One animal died of intractable ventricular fibrillation after repositioning of a guidewire with its catheter tip in the left ventricle. In addition, technical failure occurred in 2 pigs (supracoronary group) as a result of stent twisting ( $III^\circ$ ) in the ascending

aorta. Therefore the length of the stent was increased from 21 to 28 mm, except in the subcoronary group. Afterward, no twisting occurred in subsequent animals. Eleven animals were analyzed after successful implantation. Surgical preparation, advancement of the catheter delivery system, and deployment of the valved stent were well tolerated in all but 2 animals, one with ventricular tachycardia and one with reversible ventricular fibrillation associated with placement into the ascending aorta. Bleeding caused by insertion of the catheter delivery system into the iliac artery or infrarenal aorta was controlled easily.

**Duration of deployment.** The duration of deployment of the valved stents was  $1.7 \pm 1.2$  minutes on average. Differences between groups were not revealed.

**Assessment of transvalvular gradient.** At the end of the observation period, the valved stents did not reveal significantly higher transvalvular gradients (mean end-systolic  $\Delta p_{\max}$ :  $5.4 \pm 3.3$  mm Hg for the descending aorta group,  $5.4 \pm 1.3$  mm Hg for the supracoronary group, and  $5.5 \pm 1.1$  mm Hg for the subcoronary group) compared with their in vitro gradients.

**Evaluation of valvular opening and closure.** Two-dimensional echocardiography demonstrated complete valvular closure and opening ( $0^\circ$ ) in all 5 analyzed cases.

**Blood-flow characteristics.** Laminar blood flow was observed in 5 of 5 cases by using color Doppler ultrasonography to examine the transvalvular blood flow.

**Regurgitation and paravalvular leakage.** Angiography indicated no jet of regurgitation ( $0^\circ$ ) in 8 and mild ( $1^\circ$ ) regurgitation in 3 animals (2 in the supracoronary group and 1 in the subcoronary group). Color Doppler ultrasonography revealed no regurgitation in 5 of 5 cases. Paravalvular leakage (observed by means of IA-DSA) occurred in none of the descending aorta group and in one animal of the subcoronary and one of the supracoronary group. In contrast, color Doppler ultrasonography showed minor paravalvular leakage in 1 of 5 cases (descending group).

**Macroscopic analysis.** Good positioning ( $0^\circ$ - $1^\circ$ ) of the valved stent was reached in 8 of 11 cases. Two valved stents had 5 to 10 mm of distance ( $II^\circ$ ) and 2 valved stents had more than 10 mm of distance ( $III^\circ$ ) from the desired position in the descending artery (close to the subclavian artery). In one animal the supracoronary valved stent was implanted 6 to 7 mm ( $II^\circ$ ) too cranial (disturbing the outflow of the truncus brachiocephalicus), and in another case it shifted 2 to 3 mm ( $I^\circ$ ) toward the aortic arch. In the subcoronary group in one animal the valved stent was implanted 2 to 3 mm too proximal into the left ventricular outflow tract.

Macroscopic findings at autopsy demonstrated that the anchoring barbs of all stents were sufficiently embedded into the aortic wall in the descending aorta group ( $0^\circ$ ). In the ascending aorta group, in 2 cases the valved stent was sufficiently anchored in the aortic wall or the left ventricular

outflow tract ( $0^\circ$ ), whereas 2 of the supracoronary group were not fully embedded ( $I^\circ$ ) because of minimal shift in the lumen. In the subcoronary group, in one animal only the distal barbs were anchored, whereas the proximal barbs did not reach the wall of the left ventricular outflow tract because of the positioning of the stent.

Morphologic damage did not occur in any of the placed stent assemblies ( $0^\circ$ ). The valves inside the stents were completely free of thrombus, except in one case ( $I^\circ$ ) in the subcoronary group, which presented a thrombus ( $2 \times 3$  mm) between the stent and the outflow tract. No aortic dissection, hematoma, or bleeding into the aortic wall was macroscopically seen in any of the pigs.

## Discussion

This study introduces a new construction of a collapsible, sutureless, bioprosthetic aortic valve integrated into a nitinol stent for transluminal application. The ability to reduce the external wall of the homologous valve allowed us to reduce the diameter of the stent to a size that allowed transluminal delivery without interfering with the function of the valve. We chose this design because it passes through a relatively small introducer system. The valved stent was inserted by using a delivery technique through a self-constructed, flexible catheter (22F in the proximal portion) through the infrarenal aorta or iliac artery because the femoral arteries in pigs are only 2.5 to 4 mm in diameter, which is in contrast to those of 7 to 9 mm in human subjects. Although this catheter size required retroperitoneal preparation and arteriotomy in pigs, it could be performed through a relatively small incision in the human groin. In the future, further miniaturization of the compressed valve could even allow a consistent percutaneous delivery. We used biologic (homologous and pericardial) valves in this study, whereas other types of foldable valves may also prove suitable (eg, the tricuspid polyurethane valve).<sup>7</sup> In this preliminary study we analyzed several features of the newly designed valved stent.

## Mortality and Complications

First, 30 pilot studies served for the development of a suitable catheter delivery system, an optimal handling of the material, an anchoring mechanism, and a suitable visualization method. These pilot animals had a high complication and mortality rate (83%) caused by stent twisting, dislodgement, difficulties of advancing the catheter delivery system (around the aortic arch), vessel perforation (because of rigidity of the delivery system), and myocardial ischemia (caused by placing the stent too close to the coronary ostia).

However, after improvement of material and insertion techniques among the 14 animals of this study group, all but one survived the procedure and the following observation period. More secure and easier placement of the aortic valve

assembly was accomplished after increasing the height of the stent (except for in the subcoronary group) in the ascending aorta. Furthermore, the anchoring barbs were necessary for stable deployment into the aorta.

### Transvalvular Gradient and Regurgitation

Many authors have highlighted the necessity for caution in using *in vitro* results to assess a valve's performance *in vivo*.<sup>8,9</sup> Therefore the valved stents, which revealed a pressure gradient of less than 7 mm Hg and a regurgitation of I° or less in the circulatory system, were used and retested *in vivo*. As the gold standard, the natural aortic valve provides minimal obstruction to the ventricular outflow during systole. In this sense it is considered to provide maximum forward flow efficiency. By comparison, the prosthetic or bioprosthetic valve is more obstructive and hence less efficient than the natural valve. In all our experiments, transvalvular pressure measurements indicated very low gradients several hours after placement of the valved stents. Relevant stenotic transvalvular gradients were also not observed in other experimental studies<sup>1,3,4</sup> in which smaller series of valved stents were analyzed.

Although the size of the valved stent correlated with the width of the aorta (determined with IA-DSA) and body weight, mild regurgitation was observed in 3 of 11 cases and mild paravalvular leakage in 2 of 11 cases, mainly caused by a slightly tilted stent that could not be perfectly expanded in the ascending arched aorta. These findings demonstrate that the valved stent effectively prevents regurgitation when the valve has an optimal size and is anchored properly in the descending aorta group.

In general, a suitable positioning (which might require a slightly different stent design with the same valve design as proposed below) and size of the valved stent leads to unobstructed forward blood flow and prompt opening and closure. Therefore more experience is required with the angiographic sizing used in this study and also with echocardiographic sizing for subsequent insertion of valved stents. Furthermore, one can postulate that the dynamic interaction between the valved stent and aorta (which changes its size during the cardiac cycle) could be another reason for the mild regurgitation observed in these 3 animals, as opposed to the *in vitro* data of these same 3 valves, which were collected in a rigid system.<sup>9</sup>

### Stent Design

In 1992, Dake and coworkers<sup>10</sup> started implantations of stent graft prostheses in patients with thoracic aneurysms. Since then, improvements in interventional catheterization and stent technology have made percutaneous stent placement a routine procedure, and more than 20 noncovered and covered stent designs have been developed to fit the multiple cardiovascular indications.<sup>11</sup> Therefore experience with

this kind of introducer system and different stent assemblies has been already acquired in other applications.

### Limitations of the Study

Continuous electrocardiographic, hemodynamic, and pulse oximetric monitoring was used throughout the procedure. Nevertheless, hemodynamic parameters and global cardiac function should be analyzed in detail in further studies (eg, to describe the changes during implantation and deployment of valved stents). Changes of the coronary blood flow after supracoronary valved stent implantation should be included in subsequent studies. Unfortunately, this has also not been performed in other studies.<sup>1-4</sup> Because of the echo-dense structure of the stent, echocardiographic assessment could not adequately be performed in all cases.

Because of the unfeasibility of the aortic valved stent implantation into the aortic anulus, the valve had been evaluated in the subcoronary and supracoronary position. This experimental positioning of the valved stent was only used because native porcine leaflets were not removed in this study and will therefore occlude coronary ostia. As Andersen and colleagues<sup>1</sup> already showed in their porcine model, the implantation of a valved stent into the annular position is impossible because of the restriction of coronary blood flow.

In contrast, Pavcnik and colleagues<sup>2</sup> experimentally showed that transannular placement of a prosthetic caged-ball aortic valve in mongrel dogs is feasible. Their ring assembly was successfully placed below the ostia of coronary arteries and was securely anchored against the anulus of the aorta by the barbs, and no damage to the surrounding structures was macroscopically noted.

The degeneration of bioprosthetic valves has been widely studied in recent years. Various causative factors are involved that influence the durability of the valve to different degrees.<sup>12</sup> Because only acute studies were performed, the long-term durability of this kind of aortic valved stent is unknown. Questions regarding thrombogenicity, neointimalization, calcification, stability of position, histomorphologic examination, and function during long-term follow-up should be addressed. Percutaneous implantation is one of several steps toward an ideal percutaneous aortic valve replacement (ie, in human subjects with a calcified stenotic aortic valve). Development of various techniques for implementing this replacement should be also considered. Percutaneous aortic valve ablation techniques for aortic stenosis, a stable scaffold enabling those intra-aortic procedures, filters avoiding systemic embolization, and circulatory support during percutaneous aortic valve ablation and implantation with a femoro-femoral bypass and left ventricular venting should be developed. In our short-term study the duration of deployment was about 2 minutes. Nevertheless, a longer operation time (>3 minutes) in the ascending aorta will be necessary for percutaneous aortic valve ablation and



implantation, and therefore hemodynamic instability can be expected. More complex procedures at the native aortic valve using ablation techniques should only be performed with a circulatory support.

Future techniques will allow transluminal aortic valve ablation, which will be the biggest challenge of this approach. Different ablation devices have to be tested to achieve this. Preliminary in vitro studies of our laboratory demonstrated the possibility of ablating human calcified aortic valves with 3 different types of lasers (CO<sub>2</sub>, Hol:YAG, and Erb:YAG lasers). Complete ablation of each aortic cusp took 2.5 hours with the CO<sub>2</sub> laser and 1 hour with the Hol:YAG laser. The erbium laser was checked for the excision of a cusp. This also took 1 hour (unpublished data). In subsequent studies ablation time will be reduced by optimizing the laser parameters. Examination of the remaining debris solution of the lasered aortic cusps indicated debris particles with a size between 4  $\mu$ m and 1 mm. Therefore these particles have to be eliminated by using a filter system, which has not yet been developed.

Although a great deal of work remains to be done, these preliminary results indicate that the development of a prosthetic aortic valved stent for transluminal placement is feasible.<sup>1-5</sup> Probably this valved stent would be applicable to aortic insufficiency caused by valves that are pliable enough to be displaced against the aortic wall in the subcoronary region but do not adequately conform to it. In patients with fulminant endocarditis and aortic insufficiency, the valved stent might be implanted in the descending aorta for hemodynamic stabilization. Another possibility will be the implantation of a valved stent into the pulmonary position, which has already been shown by Bonhoeffer and colleagues.<sup>4</sup>

An ideal aortic valved stent may be achieved for long-term use by individually lining the entire aortic root (including the sinus), ascending aorta, and aortic arch with stent material (including a bioprosthesis) to avoid any shift caused by shear stress, with individually designed marked wholes for the coronary and supra-aortic arteries. An additional anchoring of stents into the supra-aortic vessels and the ascending valved stent should be considered.

## Conclusion

The short-term effectiveness of transluminal aortic valve implantation to the descending and ascending aorta was evaluated and demonstrated good preliminary results in anesthetized pigs. The future opportunity to implant aortic valves percutaneously in human subjects will be dependent on the development of a transluminal ablation technique with a very low debris rate, a good filtration method avoiding emboli, and an adequate circulatory support system.

We thank Gudrun Heinrichs, Dr Peter Osypka, and Christoph Benk for their technical advice; Manfred Olschewski for his sta-

tistical analysis; Ulrich Matern, MD, for his scientific input; and Kerstin Schlegel, Jeanette Schreiber, Tim Attmann, Florian Jentzmik, Eric Haffner, and Alexander Thiem for their operation assistance.

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## Discussion

**Dr Alain F. Carpentier** (Paris, France). Of course, this is a very appealing approach, and I congratulate you for the effort you made to develop stentless, minimally invasive valve implantation. However, if you think about the indications and knowing what we know in cardiac surgery, I think we could say that this technique, if it works one day, will be particularly indicated in elderly patients with calcified aortic stenosis. And as surgeons, we know that these calcified lesions are extremely difficult to remove without fragmentation and without leaving some pieces of calcium, which could migrate. Now, you mention this problem, but you did not tell us what solutions you foresee to solve and prevent embolization, which is key for the success of this operation.

A second aspect is this: We also know from clinical practice, that if you leave even a small peripheral leak, it has some very often important deleterious effect, even a rather small leak, either hemolysis or insufficiency. Knowing that you will never be able to remove all the calcium formation, then you have a high risk of having peripheral leak. How can you solve that problem?



**Dr Lutter.** Thank you very much for your kind remarks, Dr Carpentier.

With respect to your first remark, to ablate the calcified, stenotic aortic valve will be a challenge, and this has been a big problem up to now. We have performed several pilot ablation studies and can say that different lasers can microscopically ablate the aortic valve, but we have not had techniques up to now that can, in the ascending aorta, ablate the calcified valve.

So you are right also with your second remark regarding the small leaks and the possible upcoming insufficiency if you perform a valve stent implantation in a calcified anulus. And you have to be sure that every particle, every embolus that might come up to the supra-aortic vessels, you have to filter, and this is truly a lot of work to be done. Therefore, we think that, as surgeons, we should start with this work; otherwise the cardiologists will start with this problem. Therefore, we think we have to have a scaffold in the ascending aorta, with which we can properly work.

**Dr Hani Shennib** (*Montreal, Quebec, Canada*). Dr Lutter, is this technology good or bad for surgeons? Could you see that

this will ultimately be an interventional cardiology type of technique?

And also, when you propose that a femoro-femoral bypass would be a way to support the heart, is there a possibility of looking at coupling this with drugs, such as adenosine, to arrest the heart or to control hypertension?

And the other part of the question is that when you solve the problem, you create another problem. Is embolization control an issue here, and would you couple this with other technologies, such as protection catheters?

**Dr Lutter.** Regarding your first remark, is it bad or not for surgeons, this is a question for the future, and I cannot answer it now. So whether you can do it on a beating heart or not, that will be seen in the future.

And with respect to your second remark, regarding embolization control, we do not have it right now because if you have a total and very good filter in your ascending aorta, up to now, you have such resistance in the ascending aorta, which you cannot have on a beating heart.

### Targeted

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